REMARKS

In response to the present action, Applicant has amended Claims 29-31 and cancelled withdrawn Claims 14-27 without prejudice to filing those claims in a divisional application. Accordingly, Claims 29-34 are pending. None of these amendments presents new matter. Favorable reconsideration and allowance are respectfully requested.

Applicant thanks the Examiner for the courtesy of a telephone interview on May 5, 2005. As in the interview, Applicant believes it helpful to begin this response by addressing the last rejection of the office action first as this clarifies the claimed subject matter.

New Matter Rejection

Claims 29-34 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which the Examiner considered to be new matter. In particular, the Examiner requested that Applicant point out the support in the specification for the phrases "antibody specific for GM-CSF" and "antibody specific for M-CSF." Applicant respectfully directs the Examiner to Page 4, lines 10-14, wherein it states that "the present invention provides a composition comprising two immunointeractive molecules wherein one is specific for M-CSF and another is specific for GM-CSF . . . ." Additionally, at Page 10, line 21, the specification indicates that immunointeractive molecules include antibodies ("The molecules making up an agent include . . . immunointeractive molecules (e.g., antibodies) capable of interacting with a colony stimulating factor . . ."). Finally, antibody specificity is a well known term of art which usage is clearly and readily understood by those of skill in the art to mean that the antibody interacts with or binds to a particular antigen in a direct and specific manner –in this case the

antigens are the cytokines GM-CSF or M-CSF. Hence, the subject matter of the claims is supported in the specification and does not present new matter.

The Examiner also suggested that the phrase "antagonized the effects of M-CSF or GM-CSF on cells" represents an unsupported departure from the specification. This phrase, or a close variation of it, appears as part of a longer phrase throughout the specification and original claims as "antagonized the effects of M-CSF or GM-CSF on cells of the monocyte/macrophage lineage." To expedite prosecution, Applicant has amended the claims back to their original, previously-acceptable form to thereby recite the entire quoted phrase in Claims 29 and 30. This amendment means that the appearance of the above, underlined words in Claim 31 is redundant, so these words have been removed from Claim 31.

Accordingly, withdrawal of this rejection under 35 U.S.C § 112, first paragraph, is deemed proper, and such action is respectfully requested.

The 102(a) rejection

According to the present Office Action, Claims 29-33 remain rejected under 35 U.S.C. § 102(a) as allegedly anticipated by WO00/09561 (the WO '561 reference) as evidenced by Bost *et al.* (Immunol. Invest. 1988; 17:577-586) and Bendayan (J. Histochem. Cytochem. 1995; 43:881-886), hereafter Bost and Bendayan, respectively (page 2, ¶4). Specifically, the Examiner appears to have taken the position that the WO '561 antibodies are specific for GM-CSF. However, as discussed in the telephone interview, this is not the case. In particular, the only antibodies disclosed and enabled by the WO '561 reference bind to (*i.e.*, are specific for) the common beta chain that is part of the IL-3, GM-CSF and IL-5 receptors (*i.e.*, the β_c chain). Such antibodies

are anti-receptor antibodies and are distinct from anti-ligand antibodies, which are representative of the antibodies used in the present invention.

An examination of the WO '561 reference establishes that the subject matter thereof relates only to anti-receptor antibodies based at least on the following information:

(1) The background section of the WO '561 reference indicates that the IL-3, GM-CSF and IL-5 cytokine receptors are composed of two chains: an alpha chain that is ligand specific (*i.e.*, a chain which determines receptor specificity) and the β_c chain which is shared by the three receptors (Page 1, lines 33-35).

(2) The "Summary of the Invention" in the WO '561 reference states that that invention resulted from the isolation of a monoclonal antibody (BION-1) raised against the membrane proximal domain of the β_c chain (Page 3, lines 10-20), hence the antigen that reacts with BION-1 antibody is from one chain of the cytokine receptor. More detail in this regard is provided by the Examples which describe exactly how BION-1 was produced (Page 18, lines 1-11).

(3) The invention of the WO '561 reference only relates to antibodies that have the characteristics of BION-1 and BION-1 is the only example of such an antibody that is disclosed in the WO '561 reference.

(4) The data characterizing BION-1 demonstrate (a) that BION-1 binds to cell lines that express the GM-CSF receptor, the IL-3 receptor or the IL-5 receptor (Page 18, lines 13-18); and (b) that BION-1 immunoprecipitates the β_c chain (*see, e.g.*, Fig. 2 and the text at Page 18, lines 20-35). In fact, the WO '561 reference explicitly states that the "antigen recognized by BION-1 was confirmed to be domain 4 of β_c" (Page 18, line 20).

Hence, the antibodies described in the WO '561 reference are specific for a portion of the GM-CSF receptor (which is shared in common with the IL-3 and IL-5 receptors) and are not specific for its ligand GM-CSF (or IL-3 or IL-5) .

The antibodies described in the WO '561 reference are distinct from those described in the present invention and there is no teaching or suggestion in the WO '561 relating to the antibodies used in the presently claimed invention; therefore, this reference fails to teach every element of the presently claimed subject matter and can not anticipate the subject matter of Claims 29-33.

Finally, Applicant wishes to acknowledge and rectify an error in the previous response that may have lead to some confusion regarding the nature of the antibodies disclosed in the WO '561 reference. In the previous response, Applicant stated that the "antibodies disclosed in the WO '561 reference *bind to the common beta chain (β_c) of IL-3, GM-CSF and IL-5*, and thus represent an antibody reactive with multiple cytokines" (emphasis added, Page 9, last paragraph). In fact, what should have been stated is that those antibodies bind to the common beta chain of the IL-3, GM-CSF and IL-5 receptors, making the comment about cross-reactivity irrelevant. Applicant sincerely regrets the mistake and believe that the present record now correctly describes the content of the WO '561 reference and how it differs from the presently claimed subject matter.

Accordingly, Applicant respectfully requests withdrawal of this rejection under 35 U.S.C. § 102(a).

The 102(e) rejection

Claims 29-33 remain rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 5,837,460 to Von Feldt *et al.* (the '460 patent).

It is clear from the foregoing that the presently claimed subject matter is directed to methods of treating inflammation using antibodies specific for GM-CSF, M-CSF or a combination of such antibodies.

The '460 patent, in contrast, is directed to a method of generating peptide mimetics (Col. 2, lines 20-54) and discloses that those peptide mimetics exhibit the activity of a biologically-active protein, with preparation of peptide mimetics for GM-CSF serving to exemplify that method. According to the '460 patent, the procedure to obtain such peptide mimetics involves generating first antibodies against biologically-active GM-CSF. Those first generation antibodies (also termed therein as "anti-biologically active protein antibody," *see*, col. 5, lines 7-11 and lines 63-65) are then isolated and used as immunogens to produce a second generation of antibodies. Once the second generation antibodies are obtained, cDNA encoding those antibodies is isolated, cloned and sequenced. This sequence information provides the amino acid sequence of the second generation antibodies' CDR domains[1] and it is that sequence from which the peptide mimetics are derived. The peptide mimetics are thus peptides of 5-30 amino acids having a sequence corresponding to a CDR region of the second generation antibodies. According to the '460 patent, these small peptides mimic GM-CSF activity and, when acting as antagonists of GM-CSF, could have utility as anti-inflammatory agents. However, the only data presented in this regard shows that certain peptide mimetics, and certainly not all peptides obtained by this method, inhibit the proliferation of GM-CSF-dependent cell growth in cultured cells (Example 2, especially at col. 21, lines 19-64).

Importantly, the '460 patent does not teach a use for either the first generation or second generation antibodies in the treatment or amelioration of inflammation. Rather, the '460 patent

[1] CDR domains are the "complementarity determining regions" of an antibody and represent that portion of the antibody that has the amino acid residues that bind to the antigen against which that antibody recognizes.

only teaches that the peptide mimetics (*i.e.*, the molecules which are considered equivalents or "copies" of GM-CSF) are anti-inflammatory agents and not that antibodies against GM-CSF (which molecules would never be considered as equivalents or "copies" of GM-CSF) have such activity or would be expected to have such activity. In fact, the '460 patent teaches away from the present invention since that patent directs those of skill in the art away from using antiboides as therapeutic agents and directs those persons to using the peptide mimetics as the therapeutic anti-inflammatory agents.

Based on the teaching in the '460 patent, it would not be obvious to use the first generation antibodies thereof as anti-inflammatory agents as provided in the presently claimed invention., especially since antibodies are much larger molecules and exert activity via a different mechanism. No where is there any disclosure, teaching or suggestion in the '460 patent that administration of antibodies specific for GM-CSF, M-CSF or both are useful to ameliorate inflammation. Accordingly, the '460 patent neither anticipates nor renders obvious the presently claimed invention. Hence, Applicant, respectfully requests that this rejection under 35 U.S.C. § 102(e) be withdrawn.

The 103(a) rejection

Claim 34 has been rejected under 35 U.S.C. § 103(a) as allegedly rendered obvious by the WO '561 reference or the '460 patent, each in view of U.S. Patent No 5,444,153 to Goss *et al.* (the '153 patent) or U.S. Patent No. 5,662,609 to Slepian *et al.* (the '609 patent).

The primary references (the WO '561 reference and the '460 patent) have been discussed above and distinguished. Neither reference provides an antibody specific for GM-CSF or that is useful for ameliorating inflammation or any teaching to that effect. Moreover, neither reference

teaches the need for such antibodies. Because the secondary references (the '153 and '609 patents) relate to methods of treating inflammatory diseases in a patient by administering specific inhibitors of u-PA, they do not ameliorate the deficiencies of the primary references. Accordingly, the secondary references neither alone or in combination the primary references fail to render obvious the subject matter of Claim 34. Applicant believes this rejection is traversed and respectfully requests withdrawal thereof.

Conclusion

In view of the foregoing amendments and remarks, Applicant firmly believes that the examined subject matter is in condition for allowance, which action is earnestly solicited. If any issues remain outstanding after consideration of this Amendment, the Examiner is invited to contact the undersigned to expedite prosecution of this case.

Respectfully submitted,

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